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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/983,025	10/22/2001	Claus Oxvig	OXVIG=1A	7756

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EXAMINER
RAMIREZ, DELIA M

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 05/18/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/983,025	OXVIG ET AL.	
	Examiner	Art Unit	
	Delia M. Ramirez	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *4/7/2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *12,18,19,30-47,49-52,55-58,62,75,83,87,90-93 and 95-109* is/are pending in the application.

4a) Of the above claim(s) *30-47,49-52,55-58 and 62* is/are withdrawn from consideration.

5)☒ Claim(s) *90-93,95,96,100 and 109* is/are allowed.

6)☒ Claim(s) *12,18,19,75,83,97-99,102 and 104-107* is/are rejected.

7)☒ Claim(s) *87,101,103 and 108* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

RD

DETAILED ACTION

Status of the Application

Claims 12, 18-19, 30-47, 49-52, 55-58, 62, 75, 83, 87, 90-93, 95-109 are pending.

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 4/7/2005 has been entered.

Applicant's amendment of claims 12, 30, 39, 49, 52, 55,58, 62, 75, 83, 90-93, 95-96, 98-100, addition of claims 101-109, and cancellation of claims 17, 70, 85, 94, in a communication filed on 4/7/2005 are acknowledged.

Claims 12, 18-19, 75, 83, 87, 90-93, 95-109 are under consideration and are being examined herein. Claims 30-47, 49-52, 55-58, 62 are withdrawn from consideration as being directed to a non-elected invention.

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Claim Objections

1. Claim 12 is objected to due to the recitation of "a polypeptide of (a)". It is suggested the term be amended to recite "<u>the</u> polypeptide of (a)" since the polypeptide has been previously defined in (a). Appropriate correction is required.

2. Claim 83 is objected to due to the recitation of "sequence which differs from said sequence (a)". For clarity and consistency, it is suggested the term be amended to recite "sequence which differs from that of the polypeptide of (a)". Appropriate correction is required.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 12, 18-19, 75, 83, 97-99, 102-103, 105-107 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

5. Claims 12 and 102 (claims 18-19, 75, 83, 103, 105-107 dependent thereon) are indefinite in the recitation of "at least 99% identical to a polypeptide of (a), but differs therefrom by one or more insertions and/or deletions and/or substitutions" for the following reasons. As written, it is unclear if the term "therefrom" refers to the 99% variant or the polypeptide of (a). Thus, one could interpret the claim to be directed to (1) a variant of the polypeptide of (a) wherein said variant results from one or more insertions and/or deletions and/or substitutions and wherein said variant is at least 99% sequence identical to the polypeptide of (a), or (2) a variant of a polypeptide having 99% sequence identity to amino acids 234-1791 of SEQ ID NO: 2, wherein said variant can have any number of insertions and/or deletions and/or substitutions. It is suggested that if the intended scope is that of interpretation (1), the claim be amended to recite "and differs from the polypeptide of (a) by one…". For examination purposes, interpretation (1) will be used. Correction is required.

6. Claims 97-99 are indefinite in the recitation of "wherein said polypeptide or a cleavable fragment corresponding to sequence (II) of said polypeptide" because it is unclear if the term refers to (1) a fragment of the portion of the claimed polypeptide encoded by the sequence of (II), or (2) the entire portion of the claimed polypeptide which is encoded by the sequence of (II). For examination purposes, meaning (2) will be used. Correction is required.

Claim Rejections - 35 USC § 112, First Paragraph

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 105-107 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claim 105 is directed in part to a polypeptide having at least 99% sequence identity to amino acids 234-1791 of SEQ ID NO: 2 wherein said polypeptide differs from amino acids 234-1791 of SEQ ID NO: 2 by insertions or deletions of 1 to 5 amino acids. Claim 106 is directed in part to a polypeptide having at least 99% sequence identity to amino acids 234-1791 of SEQ ID NO: 2 wherein said polypeptide differs from amino acids 234-1791 of SEQ ID NO: 2 by insertions or deletions of consecutive amino acids at the N- or C-terminus. Claim 107 is directed in part to the polypeptide of claim 105 wherein the insertions or deletions are made at the N- or C-terminus of amino acids 234-1791 of SEQ ID NO: 2. While there is support in page 42, lines 4-7 for insertions of 1-5 amino acids, and deletions of 1-10 or 2-5 amino acids, the Examiner has been unable to find support for deletions of 1-5 amino acids. Similarly, while there is support in page 43, line 33-page 44, line 9 for 1-10 consecutive amino acid deletions/additions at the N- or C- terminus of amino acids 234-1791 of SEQ ID NO: 2, the Examiner has not been able to find support for any number of consecutive amino acid deletions/additions at the N- or C-terminus of amino acids 234-1791 of SEQ ID NO: 2. Thus, there is no indication that the polypeptides of claims 105-107 as described above were within the scope of the invention as conceived

by Applicants at the time the application was filed. Accordingly, Applicants are required to cancel the new matter in response to this Office Action.

9. Claims 12, 18-19, 75, 83, 97-99 remain rejected and new claims 102, 104-107 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

10. This rejection has been discussed at length in previous Office Actions mailed on 2/10/2004, 9/7/2004, and 2/9/2005. It is now applied to new claims 102, 104-107 for the reasons of record and those set forth below.

11. Applicants argue that claim 12 as amended make it clear that the activity recited refers to mature PAPP-A2 and that the variants in claim 12 have high structural similarity so that they would be expected to retain its activity. Applicants also argue that the Examiner obliquely recognized that highly structural variants would retain activity based on the statement in the Advisory Action mailed on 2/9/2005 indicating that "the limitations recited in i)-iii) are not required for the polypeptide being claimed. Applicants submit that the functional limitation recited has been placed to provide utility to the claimed polypeptides and that if the claimed polypeptides were not proteolytically active, they could still have utility in an assay due to their ability to be recognized by a PAPP-A2 antibody. Furthermore, Applicants contend that "95% sequence identity" would also be permitted according to the Written Description Training Materials and that the PTO has decided that it can live with the risk that a %5 modification could be engineered to add a new activity.

12. Applicant's arguments have been fully considered but are not deemed persuasive to overcome the rejection of claims 12, 18-19, 75, 83, 97-99 or avoid the rejection of new claims 102, 104-107. Claims

12, 18-19, 75, 83, 97-99, 104-107 are directed in part to a genus of polypeptides having any biological function which are at least 99% sequence identical to amino acids 234-1791 of SEQ ID NO: 2, or comprise a sequence which is at least 95% sequence identical to amino acids 234-1791 of SEQ ID NO: 2. Claim 102 is directed in part to a polypeptide of any function having at least 99% sequence identity to the polypeptide consisting of amino acids 234-1791 of SEQ ID NO: 2. No limitation regarding enzymatic activity or the ability to bind a particular antibody is recited in claim 102. It is noted that while claims 105-107 recite limitations in regard to the insertions/deletions that are encompassed by the claims, these limitations do not exclude substitutions and do not limit the genus of polypeptides to just variants having insertions at the N- or C-terminus of the polypeptide consisting of amino acids 234-1791 of SEQ ID NO: 2, such that the variants contain at least amino acids 234-1791 of SEQ ID NO: 2, or lack consecutive amino acids at the N- or C- terminus of the polypeptide consisting of amino acids 234-1791 of SEQ ID NO: 2. Also, it is noted that claim 12, from which the instant claims depend, allow for substitutions due to the recitation of "and/or substitutions" in claim 12. The Examiner acknowledges the amendments made to the claims. However, the Examiner disagrees with Applicants contention that the variants recited are expected to retain activity. As indicated previously, the art clearly teaches examples where 1 to 4 amino acid substitutions can result in a change in enzymatic activity, even when conservative substitutions were made. See, particularly, the teachings of Witkowski et al., Seffernick et al., and Broun et al. et al. Therefore, a genus of polypeptides having at least 99% sequence identity to amino acids 234-1791 of SEQ ID NO: 2, or a genus of polypeptides comprising a sequence which is at least 95% identical to amino acids 234-1791 of SEQ ID NO: 2, can potentially have biological functions which are not those of a polypeptide consisting of amino acids 234-1791 of SEQ ID NO: 2. These additional functions have not been disclosed in the specification or the art.

In regard to the Examiner's statement in the Advisory Action mailed on 2/9/2005, it is noted that the statement in no way is a recognition that that highly structural variants would retain activity. The

statement was made solely to indicate that the genus of polypeptides claimed did not necessarily have to encompass polypeptides having the limitations recited in i)-iii) of claims 97-99 as presented in an After Final amendment filed on 1/5/2005 due to the recitation of "wherein said polypeptide or a cleavable fragment corresponding to sequence (II) of said polypeptide". Only the cleavable fragment had to meet the limitations recited in i)-iii). The term "not required" as used in the statement made by the Examiner was clearly not intended to refer to enzymatic activity, nor was the statement made in reference to patentability (i.e. not required to be patentable) . The sole purpose of the statement was to indicate what was encompassed by the claims. This is even more evident if the sentences following the statement are considered.

In regard to Applicant's arguments indicating that if the claimed polypeptides were not proteolytically active, they could still have utility in an assay due to their ability to be recognized by a PAPP-A2 antibody, it is noted that such utility would not be considered specific since any protein which has epitopes recognized by an antibody can be used in an assay to be recognized by the antibody. In regard to Applicant's arguments of what has been deemed adequately described in the Written Description Training Materials, it is noted that the example provided in the Training Materials recites 95% identity and a specific enzymatic function, therefore, contrary to Applicant's assertion, 5% structural variability and no disclosed function is not deemed adequately described. It is reiterated herein that while it is agreed that the genus of polypeptides claimed include variants with an enzymatic function, i.e. proteolytic activity against IGFBP-5, the claims also encompass variants of unknown biological function. The specification discloses a single enzymatic activity and does not provide any teaching as to which amino acids can be modified as recited to create variants having 95% or 99% sequence identity to amino acids 234-1791 of SEQ ID NO: 2 and still display proteolytic activity against IGFBP-5. While it is agreed that (1) variants having the recited % sequence identity wherein the modifications are made outside of the region corresponding to amino acids 234-1791 of SEQ ID NO: 2 would be adequately

described since the specification teaches that this region possesses the proteolytic activity recited and it is expected that a fusion protein comprising this region would retain the proteolytic activity, and (2) variants having the recited % sequence identity wherein the modifications consist solely of deletions of a very small number of consecutive amino acids at the N- or C-terminus of amino acids 234-1791 of SEQ ID NO: 2 would also be adequately described as long as the deletions do not affect the proteolytic activity, no information is provided in regard to how this enzymatic function is affected if modifications are made within amino acids 234-1791 of the polypeptide of SEQ ID NO: 2. Therefore, for the reasons set forth above and those of record, one cannot reasonably conclude that the claimed invention is adequately described.

13. Claims 12, 18-19, 75, 83, 97-99 remain rejected and new claims 102, 104-107 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a polypeptide consisting of amino acids 234-1791 of SEQ ID NO: 2, does not reasonably provide enablement for polypeptides of any function having 99% sequence identity to amino acids 234-1791 of SEQ ID NO: 2, or polypeptides comprising an amino acid sequence 95% identical to amino acids 234-1791 of SEQ ID NO: 2. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. This rejection has been discussed at length in previous Office Actions mailed on 2/10/2004, 9/7/2004, and 2/9/2005. It is now applied to new claims 102, 104-107 for the reasons of record and those set forth below.

14. Applicants argue that either one of the limitations recited in o) or ii) is sufficient to confer utility. Furthermore, Applicants contend that considerable guidance has been provided in regard to where PAPP-A2 can and cannot be mutated, and argue that even if some of the polypeptides encompassed by the claims are inoperative, such inoperative mutants are excluded by the activity limitations. Applicants also

argue that claim 97 is defining an artificial prepeptide or prepropeptide comprising the signal sequence of (I) and the mature sequence of (II) and that the Examiner has no basis for assuming that the signal peptide of (I) will impart a significant new biological function. Similar arguments are applied to claims 98-99. Applicants submit that the claimed polypeptides are recognized by an anti -PAPP-A2 antibody and since PAPP-A2 has been found to have utility, it follows that an immunologically cross-reactive antigen has utility. In addition, Applicants submit that what is claimed is a PAPP-A2 variant and not the antibody, thus they do not need to disclose how to identify the required characteristics of the antibody for binding to the PAPP-A2 variant. Applicants indicate that the sequence of mature PAPP-A2 has been disclosed and that since many epitopes are linear and short, it is hard to believe that a significant number of mutants as claimed will lack a PAPP-A2 epitope.

15. Applicant's arguments have been fully considered but are not deemed persuasive to overcome the rejection of claims 12, 18-19, 75, 83, 97-99 or avoid the rejection of new claims 102, 104-107. Claim 102 is directed in part to a polypeptide of any function having at least 99% sequence identity to the polypeptide consisting of amino acids 234-1791 of SEQ ID NO: 2. Claims 104-107 are directed in part to the polypeptide of claim 12 with additional limitations regarding insertions/deletions. The Examiner agrees that claims 12, 18-19, 75, 83, 97-99, 104-107 encompass only those polypeptides which have either the enzymatic activity recited or the ability to bind to the recited antibody. Claim 102 does not have any limitation in regard to enzymatic activity or the ability to bind to an antibody. Contrary to Applicant's assertions, those polypeptides which lack enzymatic activity, i.e. proteolytic activity against IGFBP-5, do not have patentable utility since being able to be detected by an antibody is not considered a specific utility, and the specification fails to provide other biological functions for said polypeptides or a specific and substantial or well-established use for those inactive polypeptides. As such, it would require undue experimentation to determine a specific and substantial use for those variants lacking enzymatic activity. With regard to claims 97-99, the Examiner agrees that the addition of a signal peptide to a

polypeptide having enzymatic function is not likely to alter the enzymatic function. It is noted however that these claims also encompass polypeptides of any biological function in view of the fact that in addition to the signal peptide, they comprise variants of the mature PAPP-A2 polypeptide which lack enzymatic activity. As discussed previously, the specification provides no clue as to other biological functions for said variants and there is no disclosure of a specific and substantial or well-established utility for these inactive variants, other than being able to be detected by an antibody.

The Examiner agrees that if patentable utility is found for a polypeptide, a fragment of said polypeptide would have utility as an antigen. However, any variant of a useful polypeptide would not have patentable utility as an antigen to elicit antibodies against the useful polypeptide since a use as an antigen would not be considered specific.

The Examiner acknowledges (1) the teachings of the specification in regard to the disclosure of SEQ ID NO: 2, and (2) that the claimed invention is a polypeptide and not antibody. The Examiner also agrees that the higher the structural similarity, the higher the probability of finding more common epitopes. However, as previously indicated, the specification is silent in regard to the antibodies which are more likely to detect the recited variants with enzymatic activity or which epitopes in the polypeptide consisting of amino acids 234-1791 of SEQ ID NO: 2 are more likely to elicit antibodies which will detect polypeptides with the enzymatic activity recited. While this information is not necessary if the claims were directed to polypeptides having the recited structural limitation and the recited enzymatic activity, information regarding antibodies which are more likely to bind to enzymatically active variants or epitopes within amino acids 234-1791 of SEQ ID NO: 2 associated with the proteolytic activity recited is needed to find those variants having the only enzymatic activity disclosed in the specification. In the absence of this information, one of skill in the art would have to go through the burden of undue experimentation to determine how to use those variants which meet the structural limitations recited and bind to the recited antibodies but do not have the only enzymatic activity disclosed. Thus, for the reasons

set forth above, and those of record, one cannot reasonably conclude that the claimed invention is fully enabled by the teachings of the specification.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

16. Claims 12, 18-19, 75 remain rejected and new claims 102, 105-107 are rejected under 35 U.S.C. 102(a) as being anticipated by Farr et al. (Biochim. Biophys. Acta, 1493:356-362, October 2, 2000; cited in the IDS; SPTREMBL accession number Q9H4C9).

17. This rejection has been discussed at length in previous Office Actions mailed on 2/10/2004, 9/7/2004, and 2/9/2005. It is now applied to new claims 102, 104-107 for the reasons of record and those set forth below.

18. Applicants argue that the percent identity should be calculated over the length of the longer sequence, with end gaps included as mismatches. If percent identity is calculated this way, the polypeptide of Farr et al. would be 95.7% sequence identical to amino acids 243-1791 of SEQ ID NO: 2 (95.7% = 1554x100/1624). Applicants refer to the specification where it is stated that variants are determined on the basis of their degree of identity or their homology with a predetermined amino acid sequence, said predetermined amino acid sequence being SEQ ID NO: 2, or, when the variant is a fragment, a fragment of SEQ ID NO: 2. According to Applicants, any subsequence, even one amino acid, would be characterized as having 100% identity to the longer sequence. Applicants submit that one sequence may vary from another not only by simple replacement of amino acids but also by insertions or deletions. It is Applicant's contention that in calculating percent identity with mature PAPP-A2, it is

necessary to take into account the addition of residues and not just the deletion or substitution of residues. Therefore, the length of the longer sequence should be included in the denominator. Applicants also indicate that the claims as amended appear not to be anticipated by the mature PAPP polypeptide of Farr et al., which is 1542 amino acids long and corresponds to amino acids 250-1791 of SEQ ID NO: 2.

19. Applicant's arguments have been fully considered but are not deemed persuasive to overcome the instant rejection. New claim 102 is directed to a polypeptide having at least 99% sequence identity to a polypeptide consisting of amino acids 234-1791 of SEQ ID NO: 2. New claim 104 is directed to the polypeptide of claim 12 wherein the amino acid sequence of said polypeptide differs from amino acids 234-1791 of SEQ ID NO: 2 by amino acid substitutions. New claim 105 is directed to the polypeptide of claim 12 wherein the insertions/deletions vary from 1 to 5 amino acids. New claims 106-107 are directed to the polypeptides of claims 12 and 105, respectively, wherein the insertions/deletions are of consecutive N- or C-terminal amino acids. As indicated previously, the % identity calculation should take into consideration the fact that the identity recited is in reference to amino acids 234-1791 of SEQ ID NO: 2 (1558 amino acids). Moreover, as pointed out by Applicants, the specification teaches that when variants are a fragment, variants are determined on the basis of their degree of identity to a fragment of SEQ ID NO: 2. In the instant case, the variant taught by Farr et al. is a "fragment" since the polypeptide of SEQ ID NO: 2 (1791 amino acids long) comprises all of the polypeptide of Farr et al. (1624 amino acids) except for 4 mismatches. Those 4 mismatches (substitutions) are within amino acids 234-1791 of SEQ ID NO: 2. The claims encompass not only polypeptides of the same size as that of amino acids 234-1791 of SEQ ID NO: 2 but also polypeptides of different sizes as it recites limitations which would encompass additions and deletions. The claims also indicate that the reference polypeptide is one consisting of amino acids 234-1791 of SEQ ID NO: 2. Therefore, the polypeptide of Farr et al. is 99.7% sequence identical to amino acids 234-1791 of the polypeptide of SEQ ID NO:2 (99.7% = 1554x100/1558) and 99.7% sequence identical to amino acids 168-1791 of SEQ ID NO: 2 (99.7%

=1620x100/1624). The polypeptide of Farr et al. comprises an amino sequence which is at least 99% identical to that of a polynucleotide consisting of amino acids 234-1791 of SEQ ID NO: 2. Thus, in addition to anticipating claims 12, 18-19, 75, the polypeptide of Farr et al. would also anticipate the polypeptides of claims 104-107 since the polypeptide of Farr et al. differ from a polypeptide consisting of amino acids 234-1791 of SEQ ID NO: 2 only by 4 substitutions, and also due to the fact that the limitations recited in claims 105-107 do not exclude polypeptides which are different from the recited reference polypeptide due to substitutions (i.e. claims recite insertions and/or deletions and/or substitutions). In regard to the mature polypeptide of Farr et al. (1542 amino acids) corresponding to amino acids 250-1791 of SEQ ID NO: 2, the % identity of this polypeptide and one consisting of amino acids 234-1791 of SEQ ID NO: 2 (reference) is 98.7% (98.7% = 1538x100/1558) since there are four mismatches within amino acids 234-1791 of SEQ ID NO: 2. While the mature polypeptide of Farr et al. does not appear to anticipate the claims as written, the PAPP-E polypeptide of Farr et al. anticipates the claimed polypeptides as recited in the claims.

Double Patenting

20. Applicant is advised that should claim 83 be found allowable, claim 104 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). In the instant case, the limitation recited in both claims is the same and it is directed to the same polypeptide. The limitation recited in claim 104 can only limit the polypeptide of claim 12(b) since the polypeptide of claim 12(a) does not allow for any modifications due to the use of the term "consisting".

Allowable Subject Matter

21. Claims 90-93, 95-96, 100, 109 appear to be allowable over the prior art of record.

22. Claims 87, 101, 103, 108 appear to be allowable over the prior art of record but are objected to since they depend upon a rejected base claim.

Conclusion

23. Certain papers related to this application may be submitted to Art Unit 1652 by facsimile transmission. The FAX number is (571) 273-8300. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If Applicant submits a paper by FAX, the original copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office.

24. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PMR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

25. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Delia M. Ramirez whose telephone number is (571) 272-0938. The examiner can normally be reached on Monday-Friday from 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Ponnathapura Achutamurthy can be reached on (571) 272-0928. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Delia M. Ramirez, Ph.D.
Patent Examiner
Art Unit 1652

REBECCA E. PRUTY
PRIMARY EXAMINER
GROUP ~~1800~~ 1600

DR
May 9, 2005